APPMA

American Pet Products Manufacturers Association, Inc.

January 16, 1998

FDA's Dockets Management Branch [HFA-305]
Food and Drug Administration
12420 Parklawn Dr., Rm. 1-23
Rockville, MD 20857

Re: **Docket No. 97N-0217, Discussion Draft entitled "PROPOSALS TO INCREASE THE AVAILABILITY OF APPROVED ANIMAL DRUGS FOR MINOR SPECIES AND MINOR USES."**

Dear Sir/Madam:

The American Pet Products Manufacturers Association, Inc. [APPMA]is a trade association representing approximately 500 pet product manufacturers. Close to 40% of our members are small manufacturers, i.e., with gross annual sales of less than $500,000 nationally. We represent larger manufacturers as well. Our industry employs more than 250,000 individuals in the manufacturing, distribution and marketing of pet products, many of which, including remedies for nonfood fish, reptiles, birds, and small mammals, are necessary for the continued health and comfort of the pet. Additionally, a recent national survey showed that there are approximately 260 million pets in the United States and that 59% of American households have at least one pet.

First, I would like to express APPMA's appreciation to the Food and Drug Administration/Center for Veterinary Medicine [FDA] for the time and effort expended in responding to the needs of industry and the consumer for more flexible mechanisms for drug approvals for minor species. APPMA strongly supports these efforts to develop flexible mechanisms for approval of drugs for nonfood minor animal species as presented in this "Discussion Draft," particularly the alternate approval standard/expert review panels. APPMA's comment is enclosed.

APPMA's general position on this issue was provided in a detailed comment dated September 5, 1997 in response to the June 23, 1997, Federal Register document entitled "Request for Comments on Development of Options to Encourage Animal Drug Approvals for Minor Species and for Minor Uses" [62 Fed.Reg. 120, 33781]. APPMA reiterated that position in a December 23, 1997 response to the "Draft Guidance for Industry #61, FDA Approval of Animal Drugs for Minor Uses and for Minor Species" [Guidance #61].

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We again urge the expeditious passage of legislative and regulatory options that will facilitate the approval of new animal drugs intended for use in minor species and for minor uses, as contemplated in the Animal Drug Availability Act of 1996 [ADAA], particularly for the nonfood minor animal species. Drug uses in these nonfood minor animal species maintained as pets present minimal or no human health concerns. The economics of the current animal drug approval process effectively preclude FDA-approved drugs for treatment of nonfood minor species, since the standards are essentially the same for food animal species and nonfood species. This process is prohibitively expensive as applied to remedies for nonfood minor species because of the relatively small volume of sales for any one drug.

In developing new animal drug approval processes for minor species, the Food and Drug Administration [FDA] must, first and foremost, differentiate between drugs intended for food animals and those intended for nonfood animals. The nonfood minor species group should also be sub-classified to reflect the type of animals, relative abundance, and use in society. One such subgroup should be nonfood minor species animals maintained as companion pets such as birds, reptiles, amphibians, fish and small mammals (other than dogs and cats).

Furthermore, "crop grouping" should be permitted for the purpose of drug approvals for those nonfood minor animal species maintained as pets, including numerous, diverse genera and species, e.g., ornamental aquarium and garden pond fish. Any drug approval process for nonfood minor species animals which continues the use of the current species-specific regulatory approach requiring different approvals for each species will be prohibitively expensive for manufacturers and for consumers.

While APPMA's attached comments are primarily addressed to drug approvals for a subgroup of nonfood minor animal species maintained as pets [ornamental aquarium and garden pond fish], the basic concepts are applicable to other nonfood minor animal species maintained as pets. While drugs are available and approved for many animal species of higher commercial value, the economic justification for obtaining drug approvals for nonfood minor species maintained as companion pets does not exist under the current regulatory scheme because of the typically small volume of sales for any one drug. In order to permit approval of safe and effective therapeutic agents for use in these nonfood minor species, appropriate drug approval procedures must be created. Without access to approved animal drugs, these animals may experience unnecessary suffering and/or death due to diseases

which are treatable by therapeutic agents which are unavailable to the consumer solely because of the prohibitive cost of drug approvals.

The FDA's discussion draft is a big step towards taking advantage of the opportunity created by the ADAA for legislative and regulatory options that will facilitate the approval of new animal drugs intended for use in minor species and for minor uses. We urge the FDA to go forward with this draft, taking into consideration our attached comments in order to take full advantage of this opportunity to the maximum extent possible.

Again, we thank the FDA for these efforts and appreciate the opportunity to express our opinion on this critically important issue.

Sincerely yours,

Avis W. Effinger, Esq.
General Counsel

Attachment: APPMA's Comment dated January 16, 1998.

APPMA

American Pet Products Manufacturers Association, Inc.

January 16, 1998

COMMENT: Docket No. 97N-0217, **Discussion Draft entitled "PROPOSALS TO INCREASE THE AVAILABILITY OF APPROVED ANIMAL DRUGS FOR MINOR SPECIES AND MINOR USES."**

Note: As with previous comments by the American Pet Products Manufacturers Association, Inc. [APPMA] on this issue, these comments are primarily addressed to drug approvals for a subgroup of nonfood minor animal species maintained as pets, i.e., ornamental aquarium and garden pond fish. However, the basic concepts are also applicable to other nonfood minor animal species maintained as pets such as birds, reptiles, amphibians, and small mammals (other than dogs and cats).

Specific comments are generally presented in the order and under the titles provided in the "Discussion Draft." The page numbers refer to those in the version of the draft obtained through the Internet on the CVM World Wide Web site. These comments are made with the understanding that the term "minor use" includes "minor species" as stated in footnote number one of the "Summary." However, APPMA has suggested the specific reference to nonfood minor species at some particularly critical points in the document.

I. INTRODUCTION

Introductory Comment: APPMA strongly supports the efforts of the Food and Drug Administration/Center for Veterinary Medicine [FDA] to develop flexible mechanisms for approval of drugs for nonfood minor animal species as presented in this "Discussion Draft," particularly the alternate approval standard/expert review panels. Standards for nonfood minor species drugs different from those implicating human food safety are appropriate since these drugs are typically used in low concentrations and pose minimal risk to human health. APPMA offers the following comments and believes that incorporation of these recommended changes will result in a process for safe, effective, and affordable approved drugs for nonfood minor species animals maintained as companion pets such as birds, reptiles, amphibians, fish and small mammals (other than dogs and cats).

A. A SINGLE APPROVAL MODEL FOR HUMANS AND ANIMALS

Comment:

Page 3. It should be emphasized that minor species can be [rather than "are"] reservoirs and vectors for diseases affecting human and major species.

Page 5. Additional steps are required [other than flexible application of standards and policies] for product availability for minor species as well as for minor uses.

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III. OPTIONS AVAILABLE UNDER EXISTING LAWS ARE INADEQUATE

Pages 4 - 5.

Comment: APPMA strongly supports the proposition that options available under existing laws are inadequate for the approval of new animal drugs intended for use in nonfood minor species, as contemplated in the Animal Drug Availability Act of 1996 [ADAA].

B. SUPPLEMENTAL APPLICATIONS

Page 5.

Comment. While "The Modernization Act" only allows FDA to modify policy, the ADAA does provide the opportunity to allow FDA to promulgate regulatory standards for nonfood minor species drug approvals that can significantly facilitate approvals of drugs for use in these species. [APPMA's September 5, 1997 comment provided specific recommendations.]

E. INTERNATIONAL HARMONIZATION

Page 6.

Comment: It should be emphasized that expansion of activities such as exchange of information and data with foreign regulatory agencies coupled with the recognition of foreign country drug approval test results, GLP's and other related studies and citations could have a significant beneficial effect on minor use drug approval processes.

F. THE NATIONAL RESEARCH SUPPORT PROJECT #7 (NRSP-7)

Page 6.

Comment. Congress should direct the U.S. Department of Agriculture [USDA] to expand the definition of minor species served by the NRSP-7 program to include all nonfood companion animal minor species (mammals, birds, reptiles, amphibians, fish).

IV. PROPOSALS TO INCREASE THE NUMBER OF APPROVED ANIMAL DRUGS FOR MINOR USE

B. REMOVAL OF DISINCENTIVES

1. Lack of Enforcement Resources

Pages 8 - 9.

Comment: Should a position such as "Minor Use Advocate" be created, APPMA would want to continue to communicate with FDA in seeking beneficial drug approvals for nonfood minor species animals.

3. Assurance that an Existing Approval Would Not be at Risk

Page 9.

Comment: APPMA supports the amendment of the regulations to assure prospective supplemental New Animal Drug Application [NADA] sponsors for minor use drugs that their parent application will not be jeopardized by the submission of a minor use supplement. Furthermore, FDA should amend 21 CFR 514.106 to prevent critical reviews of the original major species data packages. Such amendments will facilitate access to existing data for use in approval of drugs for nonfood minor species, thus generating more affordable, approved products.

C.ENHANCEMENT OF EXISTING PROGRAMS FOR DATA DEVELOPMENT

1. Expand Established Congressional Research Funds

Page 11.

Comment: APPMA supports increasing the Saltonstall-Kennedy Grants Program funds which should be earmarked for drug research for use in aquaculture. A portion of the Hatch funds should also be earmarked for minor species drug research.

USDA ACTION:

Page 11.

Comment: APPMA supports the expansion of the scope of the NRSP-7 program to allow the funding of research for therapeutic and non-therapeutic drugs for nonfood producing animals.

2. Establish New Programs Based on the NRSP-7 Model

Page 11.

Comment. APPMA supports the use of the NRSP-7 program as a model for a separate research support program that would address the needs of the minor species and minor use groups currently excluded from NRSP-7, should the current NRSP-7 program not be expanded to allow sufficient funding of research for therapeutic and non-therapeutic drugs for nonfood producing animals.

3. Establish a Minor Use Database

Page 12.

Comment. APPMA supports the establishment of such data bases. However, it is imperative to include individuals with expertise in nonfood minor species use conditions and diseases in the list of lead-researcher practitioners from among veterinary research organizations, industry sponsors, university animal science departments, and veterinary medical schools.

D. INCENTIVES TO PURSUE MINOR USE DRUG APPROVALS

Pages 12 - 14.

Comment: The focal question should be the development of an affordable approval process for minor species and for minor uses. It would seem far more simple to provide an affordable process which allows sponsors to invest in a process of minor species drug approval.

Reduction of extensive and expensive approval procedures for nonfood minor species would be an excellent incentive. However, manufacturers of these drugs should also be provided with the same incentives given to manufacturers of human orphan drugs, e.g., tax breaks and grants.

Different strategies are certainly appropriate for food and nonfood minor animal species. FDA and minor species industry groups need to jointly determine the levels of risk involved and the approval process which is realistic. If this is done, the ability to market an approved drug is the incentive.

If the drug in question has a PMF, information should be available for reference for the minor species approval process, avoiding duplication of effort and additional cost.

E. DATA SHARING BY MAJOR SPECIES NADA HOLDERS

CONGRESSIONAL ACTION:

Page 15.

Comment. APPMA supports the proposal for amendment of the Federal Food, Drug, and Cosmetic Act [FD & C Act] to create a system whereby the Agency can

consider data underlying NADAs for major uses when reviewing NADAs for minor uses, once the drugs are subject to generic competition or have been abandoned or withdrawn. This action will benefit nonfood minor species animals and their owners by facilitating approvals of safe, effective and affordable drugs.

G. CONDITIONAL DRUG APPROVAL FOR MINOR USES INVOLVING NON-FOOD ANIMALS

Pages 16 - 18.

Comment: In the case of drug approvals for nonfood ornamental aquarium and garden pond fish, it would be best to develop a specific approval process for this subcategory of nonfood minor species, and have manufacturers proceed by submitting the appropriate data as developed by FDA and the industry. As previously stated, APPMA strongly supports the establishment of alternate approval standard/expert review panels for nonfood animal minor species as the appropriate model for the approval process.

H. ALTERNATE APPROVAL STANDARD/EXPERT REVIEW PANELS FOR MINOR USES INVOLVING NON-FOOD ANIMALS

Pages 18 - 21.

Comment: APPMA strongly supports the establishment of alternate approval standard/expert review panels for minor uses involving nonfood minor species animals and recommends changes to ensure that the mechanism will meet the goals of the ADAA.

APPMA supports the replacement of the current statutory standard for proof of drug safety, "adequate tests by all methods reasonably applicable," and for proof of effectiveness "substantial evidence ... consisting of adequate and well-controlled studies" for the nonfood minor species. Replacement of these standards is necessary to provide sufficient drugs for these animals. However, to achieve the goals of the ADAA and avoid confusion, the replacement standard should be stated solely as "sufficient evidence to convince qualified experts that the consequences of approving a drug are preferable to the consequences of not approving it."

Furthermore, APPMA strongly disagrees with the proposal for labeling and advertising to state that approval has been gained "via less stringent requirements than those of a standard NADA." This language implies that the indicated product is inferior or less safe. Rather, it would be sufficient and more accurate to require the labeling and advertising to state that approval has been gained "using the FDA alternative approval process standards and procedures, designed specifically for nonfood minor species companion animals and zoo animals."

Likewise, the use of the words "exotic pets" when describing the rationale for use of the alternate standard is misleading. Rather, the following statement more accurately reflects the categories that will benefit from this mechanism and should be used: "This alternate standard and mechanism for data review would primarily benefit zoological and wildlife species as well as minor species companion pet animals and ornamental fish."

2. Alternate Standard for Approval Under this Model

Page 19.

Comment. APPMA supports the use of an alternate standard under this model. However, this standard should be defined as "comprising sufficient evidence of

[redacted]

safeguard human health while at the same time providing industry with the capability of marketing FDA-approved drugs which prevent unnecessary pain and suffering in nonfood companion animal minor species.

- **Is the proposed process appropriately restricted to minor uses involving non-food animals?**

Comment: Yes, the proposed process is appropriately worded to restrict it to nonfood minor species animals.

I. INTERNATIONAL HARMONIZATION

Page 21.

Comment: APPMA supports FDA efforts directed towards recognition and utilization of appropriate, qualified foreign country data in the minor species drug approval process.

CONCLUSION

Legislative and regulatory options as contemplated in the ADAA are greatly needed to facilitate the approval of new animal drugs intended for use in minor species and for minor uses, particularly for the nonfood minor animal species. The "Discussion Draft" amended according to APPMA's above comments, should provide the FDA with the flexibility necessary to develop drug approval mechanisms which are appropriate for nonfood minor species and which use different standards from those applied to drugs for food animals. These new mechanisms should bring about a much needed increase in approvals for new animal drugs intended for these animals and thus address the scarcity of approved new animal drugs intended for nonfood minor species, particularly those that are maintained as pets, such as ornamental aquarium and garden pond fish.

The economics of the current NADA process effectively preclude FDA-approved drugs for treatment of nonfood minor animal species since the standards are essentially the same for food animal species and nonfood species. This process is

prohibitively expensive as applied to nonfood minor species because of the relatively small volume of sales for any one drug.

"Crop grouping" should be permitted for the purpose of drug approvals for those nonfood minor animal species maintained as pets, including numerous, diverse genera and species, e.g., ornamental aquarium and garden pond fish. Any drug approval process for nonfood minor species animals which continues the use of the current species-specific regulatory approach requiring different approvals for each species will be prohibitively expensive for consumers and for manufacturers.

The FDA's discussion draft is a big step towards taking advantage of the opportunity created by the ADAA for legislative and regulatory options that will facilitate the approval of new animal drugs intended for use in minor species. APPMA is confident that such options can provide reasonable, effective and affordable drug approval processes that will protect the public health, provide assurance of drug efficacy, and provide manufacturers of drugs with the ability to develop and market safe and effective treatments. This in turn will provide American consumers with a wider range of safe and effective products for maintenance of the health, safety and comfort of their pets. APPMA appreciates the opportunity to make comments and urges the FDA to go forward with this "Discussion Draft," incorporating the above recommendations in order to maximize this opportunity.

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